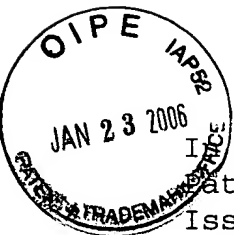


09/626566

PATENT

Rev 06/04



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Certificate

JAN 27 2006

of Correction

Re application : Qingping Jiang et al.
Patent No. : 6,783,948
Issued : August 31, 2004
Confirmation No. : 9704
For : CHEMILUMINESCENT ACRIDINIUM COMPOUNDS AND
ANALOGUES THEREOF AS SUBSTRATES OF
HYDROLYTIC ENZYMES
Examiner : Ralph J. Gitomer
Attorney Docket : CCDLT-300XX

TC Art Unit: 1651

I hereby certify that this correspondence is being deposited with
the United States Postal Service as first class mail in an envelope
addressed to: Certificates of Correction Commissioner for Patents,
P.O. Box 1450, Alexandria, VA 22313-1450 on
Jan. 19, 2006.

By: Holliday C. Heine
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
ATTN: Certificates of Correction

Sir:

In response to the letter from the Patent and Trademark
Office dated November 3, 2005 (enclosed herewith), Applicants
submit a Request for Reconsideration as follows.

BEST AVAILABLE COPY

FEB 02 2006

REMARKS

Applicants filed a Request for Certificate of Correction on May 17, 2005 (enclosed herewith) in which errors within

- (1) column 45 at line 61,
- (2) columns 47 to 50 and
- (3) columns 67 and 68 were deemed by the Patent and Trademark Office to not be in order for correction. Applicants hereby request reconsideration of the Request for Certificate of Correction in order to correct such errors.

(1) COLUMN 45 AT LINE 61

With regard to column 45 at line 61, Applicants filed a preliminary amendment on November 8, 2000 (enclosed herewith) indicating to move the figures representing the reaction scheme from the bottom of page 84 to page 85 at line 4. See page 11 of the preliminary amendment. The preliminary amendment requested that the Examiner

"[p]lease move the figures representing the reaction scheme from the bottom of page 84 to page 85, line 4, following the title of Example 10."

Applicants have also enclosed pages 84 and 85 of the above-identified patent as originally filed and marked by the Examiner, which show that Example 10 was completely removed by mistake. Thus, Applicants respectfully submit that column 45 at line 61 be corrected as indicated in the Request for Certificate of Correction to be accurate and consistent with the preliminary amendment.

(2) COLUMNS 47 TO 50

In regard to columns 47 to 50, Applicants have enclosed page 89 of the above-identified patent application as originally filed, which demonstrates that the structure noted by an arrow was published with an error. Applicants also underscore that the arrow should not be included with columns 47 to 50. Instead, Applicants submit that the error to the structure be changed as indicated in the Request for Certificate of Correction. See page 9 of the Request for Certificate of Correction. Applicants hereby request anew that the error be corrected.

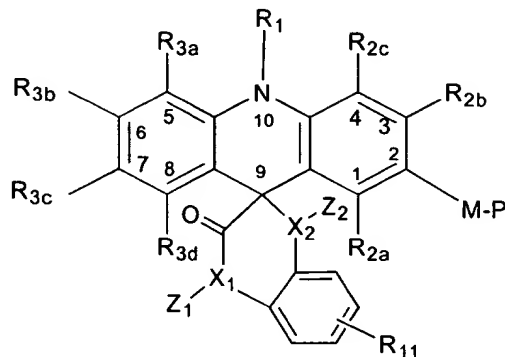
(3) COLUMNS 67 AND 68

Lastly, columns 67 and 68 were deemed by the Patent and Trademark Office to not be in order for correction. In particular, columns 67 and 68 include claim 18, which recites a structure that Applicants sought to correct in the Request for Certificate of Correction. Applicants submit that claim 18 including the correct structure was introduced in an amendment filed August 14, 2003 (enclosed herewith). See page 23 of the amendment in which present claim 18 was originally added as claim 61. Subsequently, the structure of claim 18 was incorrectly and without deceptive intent altered in an amendment filed February 24, 2004 (enclosed herewith). See page 19 of the amendment, wherein present claim 18 was added as claim 61.

To be consistent with the amendment filed August 14, 2003 in which claim 18 was originally introduced, Applicants underscore that the structure of claim 18 within columns 67 and 68 be corrected as indicated in the Request for Certificate of Correction. See page 12 of the Request for Certificate of

FEB 02 2006

Correction. Indeed, the Examiner should recognize that the structure of claim 19 in column 68 at line 28 could only be accurate should that recited by claim 18 be



as required through the Request for Certificate of Correction.

Thus, Applicants again respectfully request that the structure printed at present in claim 18 be corrected as indicated in the Request for Certificate of Correction, which entirely replaces claim 18 as published to avoid any further ambiguities or inconsistencies. The Applicants submit that no new matter would be added by such correction.

Patent No. 6,783,948
Issued: August 31, 2004
TC Art Unit: 1723
Confirmation No.: 9704

CONCLUSION

Based on the remarks presented herewith, reconsideration of the Request for Certificate of Correction is respectfully requested. Please also telephone the undersigned attorney to discuss any matter that would expedite such reconsideration.

Respectfully submitted,

Qingping Jiang et al.

By: Holliday C. Heine
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEOVICI LLP
Ten Post Office Square
Boston, MA 02109
Telephone: (617) 542-2290
Telecopier: (617) 451-0313

HCH/raw
330918

FEB 02 2006



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY OF COMMERCE AND
COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. BOX 1450
Alexandria, Va 22313- 1450
www.uspto.gov.

DATE: November 3, 2005
Patent No: 6,783,948 B1
Applicant: Jiang, et al
Issued: 08/31/04

Request for Certificate of Correction:

Consideration has been given your request for the issuance of a certificate of correction for the above-identified patent under the provisions of Rules 1.322.

Respecting the alleged error in column 45, line 61; column 47-50 and column 67-68 are printed in accordance with the record. Therefore, no correction(s) is in order here under United States Codes (U.S.C.) 254 Code of Federal Regulation (C.F.R.) 1.322.

In view of the foregoing, in this matter your request is hereby denied. A Certificate of Correction will issue for all other matters.

Further consideration will be given upon receipt of a Request for Reconsideration, which should be directed to Decisions and Certificate of Correction Branch. Requests for Reconsideration should be accompanied by additional support (e.g. copy of amendments, post card receipts. PTOL 1449 OR 892,etc.), containing requested data or changes) and /or brief statements of facts, as requested.

RoChaun Johnson for
Cecelia Newman, Supervisor
Decisions and Certificates of Correction
(703) 308-9390 ext. 119

09/626,866



PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Certificate

MAY 24 2005

In re application : Qingping Jiang, et al.
Patent No. : 6,783,948
Issued : August 31, 2004
For : CHEMILUMINESCENT ACRIDINIUM COMPOUNDS
AND ANALOGUES THEREOF AS SUBSTRATES OF
HYDROLYTIC ENZYMES
Attorney's Docket : CCDLT-300XX

of Correction

I hereby certify that this correspondence is being deposited
with the United States Postal Service as first class mail in an
envelope addressed to: ATTN: Certificates of Correction
Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
on May 17, 2005.

By: Holliday C. Heine
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney of Record

LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
ATTN: Certificates of Correction

Sir:

Enclosed are two completed copies of Form PTO 1050. It is
requested that a Certificate of Correction be issued, pursuant
to 37 C.F.R. § 1.323, to correct an inadvertent clerical mistake
that arose, in good faith, during the prosecution of the above-
identified patent.

05/20/2005 AWHDRF1 00000009 6783948

01 FC:1811

100.00 OP

-1-

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI, LLP
TEL. (617) 542-2290
FAX. (617) 451-0313

Patent No. 6,783,948
Issued: August 31, 2004

Enclosed herewith is our check in the amount of \$100.00 as payment of the fee for the above-referenced correction. In the event any additional fee is required, please charge such amount to Patent and Trademark Office Deposit Account No. 23-0804. Triplicate copies of this letter are enclosed.

Respectfully submitted,

QINGPING JIANG, ET AL.

By: Holliday C. Heine
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney of Record

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
Ten Post Office Square
Boston, Massachusetts 02109
Telephone: (617) 542-2290
Telecopier: (617) 451-0313

HCH/doc
Enclosures

321468

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

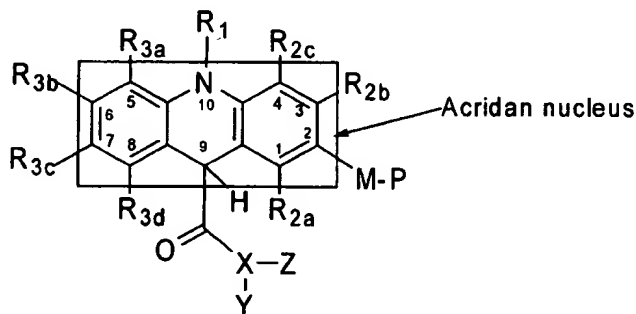
It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Front page, (57) Abstract, line 16, "it a" should read --is a--;

Column 3, line 13, "can are" should read --can be--;

Column 3, line 20, "Sasamoto at al" should read --Sasamoto et al--;

Column 15, lines 17-30, delete "Formula IV (including structure)" and insert the following Formula IV:



Formula IV

Column 15, line 34, "m group" should read --group--;

MAILING ADDRESS OF SENDER:

Weingarten, Schurgin, Gagnebin & Lebovici LLP
 Ten Post Office Square
 Boston, Massachusetts 02109

PATENT NO. 6,783,948

No. of additional copies

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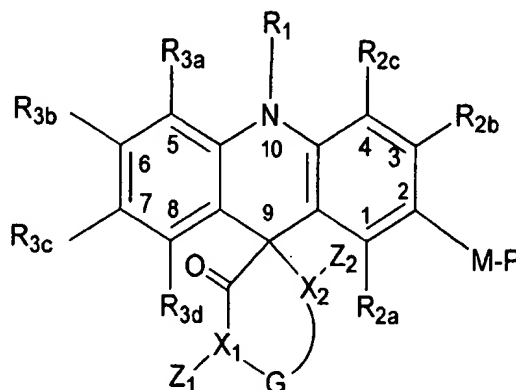


UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 15, lines 42-55, delete "Formula V (including structure)" and insert the following Formula V:



Formula V

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 Ten Post Office Square
 Boston, Massachusetts 02109

PATENT NO. 6,783,948

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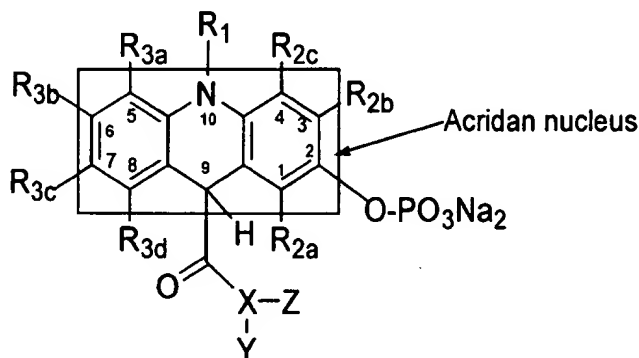
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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 16, lines 54-65, delete "Formula VIII (including structure)" and insert the following Formula VIII:



Formula VIII

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Weingarten, Schurgin, Gagnebin & Lebovici LLP
 Ten Post Office Square
 Boston, Massachusetts 02109

PATENT NO. 6,783,948

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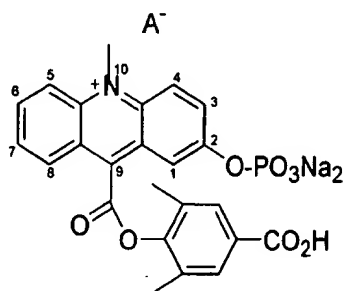
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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 17, lines 36-50, delete "1 (including structure)" and insert the following 1:



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Boston, Massachusetts 02109

PATENT NO. 6,783,948

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Page 4 of 13

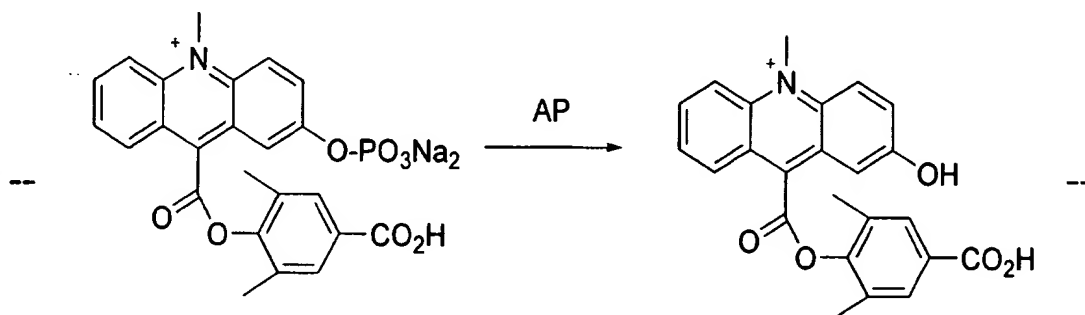
CCDLT-300XX/321273

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 18, lines 5-34, delete "Reaction B (including structures)" and insert the following Reaction B:

Reaction B

MAILING ADDRESS OF SENDER:

Weingarten, Schurgin, Gagnebin & Lebovici LLP
Ten Post Office Square
Boston, Massachusetts 02109

PATENT NO. 6,783,948

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 20, line 63, "enzyme is the" should read --enzyme in the--;

Column 22, line 59, "fulfil this" should read --fulfill this--;

Column 29, line 46, "[Krika, Clin." should read --[Kricka, Clin.--;

Column 36, line 46, "TAF/acetonitrile" should read
--TFA/acetonitrile--;

Column 36, line 50, "(DALTI-TOF):" should read --(MALDI-TOF):--;

Column 38, line 31, "TAF/" should read --TFA/--;

Column 38, line 45, "(2-Phos-NSB-DNM, 7)" should read
--(2-Phos-NSB-DMAE, 7)--;

Column 42, line 60, "10 m)." should read --10 μ m).--;

Column 45, line 61, insert the following prior to
N-(4'-Benzyloxy)phenylisatin:

-- Example 10

Synthesis of 2-OH-Spiroacridan (12) and 2-Phos-Spiroacridan
(11)

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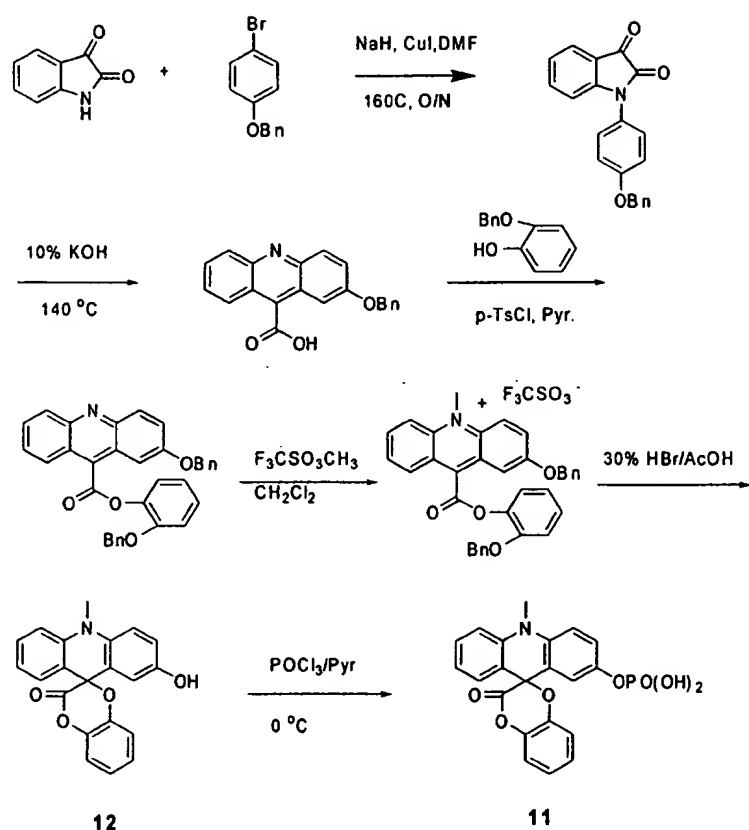


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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:



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Weingarten, Schurgin, Gagnebin & Lebovici LLP
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PATENT NO. 6,783,948

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 46, line 54, "10 μ n)." should read --10 μ m).--;

Column 46, line 61, "(M+~1)." should read --(M+1).--;

Columns 47-50, after the paragraph following Example 11, delete formulas 13 and 15 and insert the following formulas 13 and 15:

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Weingarten, Schurgin, Gagnebin & Lebovici LLP
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Boston, Massachusetts 02109

PATENT NO. 6,783,948

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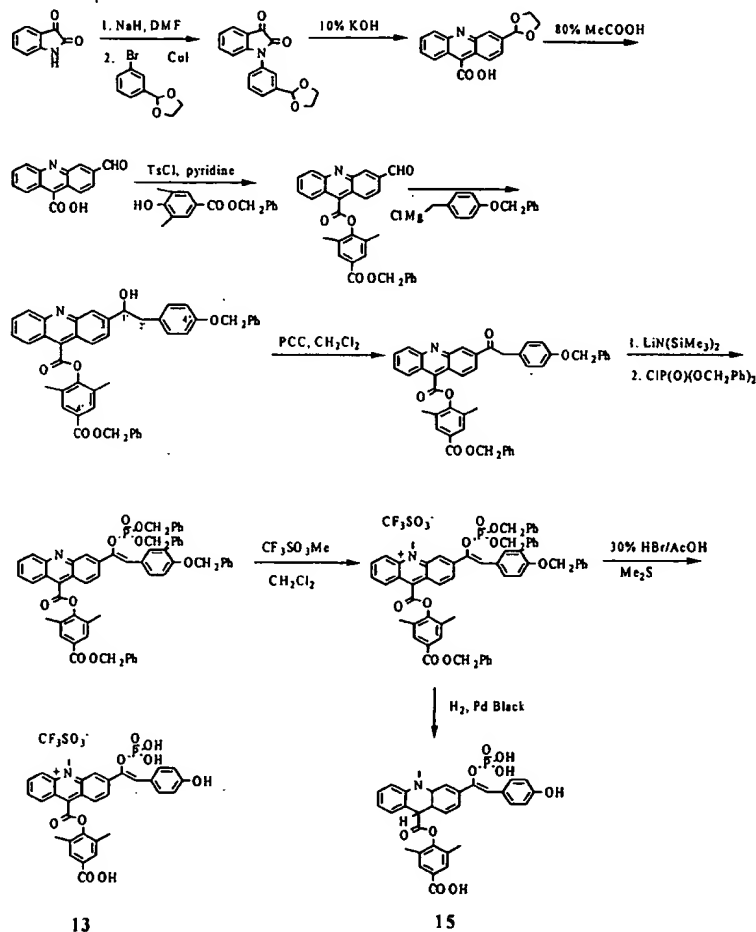


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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:



MAILING ADDRESS OF SENDER:

Weingarten, Schurgen, Gagnebin & Lebovici LLP
Ten Post Office Square
Boston, Massachusetts 02109

PATENT NO. 6,783,948

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 51, line 53, "phosphite" should read --phosphate--;

Column 57, line 18, "2-Phos-DMM" should read --2-Phos-DMAE--;

Column 60, line 50, "TSH concentration. SH" should read
--TSH concentration. TSH--;

Column 61, lines 44-62, delete "claim 3" and insert the following
claim 3:

--3. The chemiluminescent substrate of claim 1, wherein
P is PO₃B;
X is O; Y is selected from the group consisting of phenyl,
(2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl and (2',6'-dimethyl-4'-
-carboxyl)phenyl; and Z is omitted.--

Column 62, claim 8, line 48, "structures," should read
--structure--;

Column 63, claim 11, line 53, "K2, Ca" should read --K₂, Ca--;

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PATENT NO. 6,783,948

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Page 10 of 13

CCDLT-300XX/321273

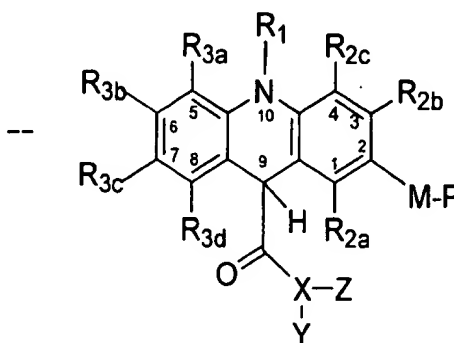
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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 66, claim 17, lines 46-59, delete the structure and insert the following structure:



MAILING ADDRESS OF SENDER:

Weingarten, Schurgin, Gagnebin & Lebovici LLP
 Ten Post Office Square
 Boston, Massachusetts 02109

PATENT NO. 6,783,948

No. of additional copies

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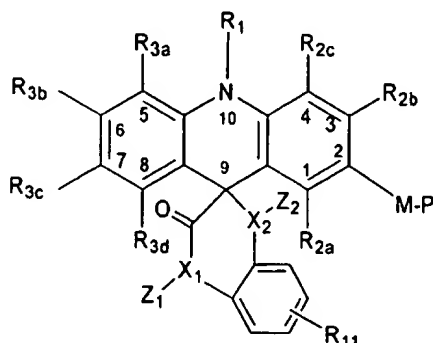
UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
DATED : August 31, 2004
INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 67-68, claim 18, delete "claim 18" and insert the following claim 18:

--18. A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

P is selected from the group consisting of PO_3H_2 , PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

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Boston, Massachusetts 02109

PATENT NO. 6,783,948

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,783,948
 DATED : August 31, 2004
 INVENTOR(S) : Qingping Jiang, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

R_1 is selected from the group consisting of methyl, sulfopropyl, sulfobutyl, sulfoalkyl, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, cyano (-CN);

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X_1 and X_2 are the same or different and are selected from the group consisting of O, N or S, such that,

when X_1 and X_2 are O or S, R_{11} is selected from the group consisting of hydrogen, -R, substituted or unsubstituted aryl, halides, nitro, sulfonate, sulfate, phosphonate, $-CO_2H$, $-C(O)OR$, cyano (-CN), -SCN, -OR, -SR, -SSR, $-C(O)R$, $-C(O)NHR$, ethylene glycol, or polyethylene glycol, where R is as defined above; and

Z_1 and Z_2 are omitted; and

when at least one of X_1 and X_2 is N, Z_1 and Z_2 are toluenesulfonyl, and R_{11} is carboxypropyl.--

MAILING ADDRESS OF SENDER:

Weingarten, Schurgin, Gagnebin & Lebovici LLP
 Ten Post Office Square
 Boston, Massachusetts 02109

PATENT NO. 6,783,948

No. of additional copies

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PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application : Qingping Jiang et al.
Application No. : 09/626,566
Filed : July 27, 2000
For : NOVEL CHEMILUMINESCENT SUBSTRATES OF
HYDROLYTIC ENZYMES AND THEIR USE IN
ASSAYS
Examiner : Unknown
Attorney's Docket : MOI-17002

Group Art Unit: Unknown

I hereby certify that this correspondence is being deposited with
the United States Postal Service as first class mail in an
envelope addressed to: Assistant Commissioner for Patents,
Washington, D.C. 20231 on 11/8/00.

By: Arthur S. Morgenstern
Arthur S. Morgenstern
Registration No. 28,244
Attorney for Applicants

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-identified
patent application as follows:

In the Claims

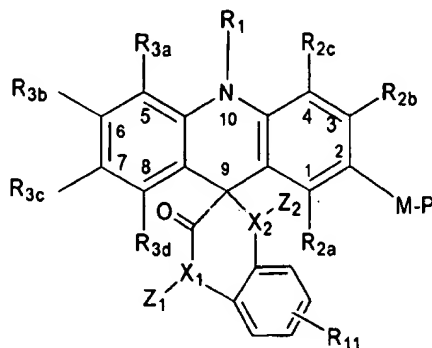
Please add the following claims:

11/15/2000 SDENB01 00000050 09626566

01 FC:102
02 FC:103400.00 OP
396.00 OP

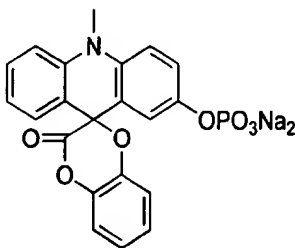


1 21. The chemiluminescent substrate of claim 20 having the
2 following structure:
3



4
5 wherein R11 is a single or multiple substitution, each
6 substituent of which is selected from the group consisting of
7 hydrogen, -R, substituted or unsubstituted aryl (ArR or Ar),
8 halides, nitro, sulfonate, sulfate, phosphonate, -CO₂H, -C(O)OR,
9 cyano (-CN), -SCN, -OR, -SR, -SSR, -C(O)R, -C(O)NHR, ethylene
10 glycol, or polyethylene glycol.

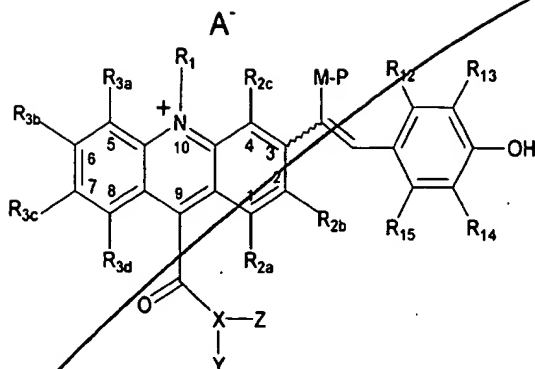
1 22. The chemiluminescent substrate of claim 21 having the
2 following structure:



3
4 23. The chemiluminescent substrate of claim 2 wherein said
5 chemiluminescent moiety Lumi is an acridinium compound having
6 the following structure:
7
8
9
10

4

Cont
a'
sub
cont

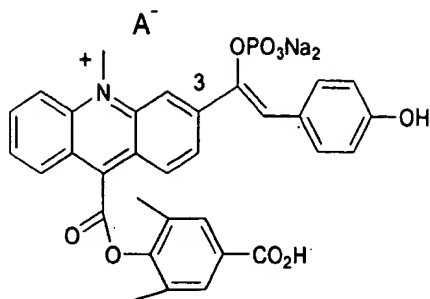


5 wherein, R_1 , R_{2a-c} , R_{3a-d} , A^- , M, P, X, Y, and Z are as defined
6 in claim 4; R_{12} , R_{13} , R_{14} and R_{15} are the same or different and
7 are selected from the group consisting of hydrogen, -R,
8 hydroxyl, amino, halides, nitro, nitroso, sulfonate, sulfate,
9 phosphonate, $-CO_2H$, cyano ($-CN$), $-SCN$, $-OR$, $-SR$, $-SSR$, $-C(O)R$,
10 and $-C(O)NHR$.

1 24. The chemiluminescent substrate of claim 23 wherein any
2 adjacent two groups of R_{12} to R_{15} can form one or more
3 additional fused hydrocarbon aromatic rings or heteroaromatic
4 rings with or without substitutions, said rings selected from
5 the group consisting of benzene, naphthlene, pyridine,
6 thiophene, furan, and pyrrole.

1 25. The chemiluminescent substrate of claim 23 having the
2 following structure:

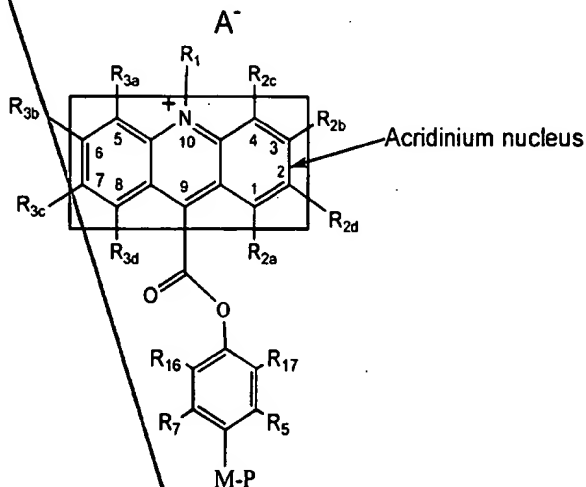
3



Cont
a' 4

1 26. The chemiluminescent substrate of claim 2 wherein said
2 chemiluminescent moiety Lumi is an acridinium compound having
3 the following structure:

4



Sub
B2

5

6 wherein, R_1 , R_{2a-c} , R_{3a-d} , R_5 , R_7 , A^- , M , and P are as defined
7 in claim 4;

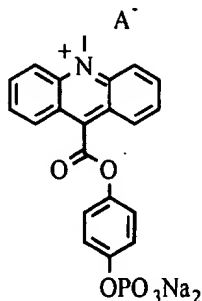
8 R_{2d} is as defined for R_{2a-c} and R_{3a-d} ;

Sub 2298
801
 R₁₆ and R₁₇ are the same or different, and are selected from the group consisting of hydrogen, methyl, alkyl with low molecular weight, and halides.

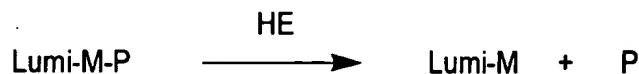
- 1 27. The chemiluminescent substrate of claim 26 wherein R₁₆ and
 2 R₁₇ are different and one of them is hydrogen.

- Cont*
a'
 1 28. The chemiluminescent substrate of claim 26 wherein both R₁₆
 2 and R₁₇ are hydrogen.

- 1 29. The chemiluminescent substrate of claim 26 having the
 2 following structure:



- 1 30. An enzymatic reaction



wherein:

- a. Lumi-M-P is a chemiluminescent substrate of a hydrolytic enzyme
 b. HE is a hydrolytic enzyme

7 c. Lumi-M is a chemiluminescent enzymatic product having
8 properties different from Lumi-M-P

1 31. The enzymatic reaction of claim 30, wherein said properties
2 are selected from the group consisting of emission wavelength,
3 quantum yield, light emission kinetics, net charge distribution,
4 dipole moment, π -bond orders, free energy, hydrophobicity/
5 hydrophilicity, solubility, and affinity.

But
a
1 32. The enzymatic reaction of claim 30, wherein HE is selected
2 from the group consisting of phosphatases, glycosidases,
3 peptidases, proteases, esterases, sulfatase and
4 guanidinobenzoatase.

1 33. An apparatus for light detection which is capable of
2 maximizing the distinction between Lumi-M from Lumi-M-P in the
3 reaction of claim 30.

1 34. The apparatus of claim 33, selected from the group
2 consisting of a luminometer, charge-coupled device camera, X-ray
3 film, and high speed photographic film.

1 35. The apparatus of claim 33, wherein the maximization of the
2 distinction can be achieved by employing optical filters.

1 36. The apparatus of claim 33, wherein the maximization of the
2 distinction can be achieved by employing a red sensitive photo
3 multiplier tube in a luminometer or back-thinned cooled charge

4 coupled device for detecting longer wavelength emitting Lumi-M
5 or Lumi-M-P.

1 37. The apparatus of claim 33, wherein the maximization of the
2 distinction can be achieved by employing a blue sensitive photo
3 multiplier tube in a luminometer for detecting the shorter
4 wavelength emitting Lumi-M or Lumi-M-P.

Cont
A!
1 38. A method of enhancing the distinction between Lumi-M from
2 Lumi-M-P in the reaction of claim 30 by treating the post
3 enzymatic reaction mixture with alkali followed by hydrogen
4 peroxide.

1 39. A method for the detection and/or quantitation of a
2 hydrolytic enzyme in a sample comprising the steps of:

3 a. providing an enzymatically hydrolyzable chemi-
4 luminescent Lumi-M-P selected from claims 1-25 capable
5 of emitting light at a first wavelength maximum when
6 chemically treated;

7 b. contacting said Lumi-M-P compound with said sample
8 containing said enzyme to allow the enzymatic reaction
9 of claim 30 to occur for the generation of said Lumi-M
10 capable of emitting light at a second wavelength
11 maximum when chemically treated;

12 c. detecting said emitted lights selectively or
13 individually as an indication of the presence and/or
14 the amount of said enzyme.

1 40. An assay method for the detection and/or quantitation of an
2 analyte in a sample comprising the steps of:

- 3 a. combining said sample with at least a member of
4 binding pair labeled with a hydrolytic enzyme to form
5 a binding complex;
- 6 b. providing an enzymatically hydrolyzable chemi-
luminescent Lumi-M-P selected from claims 1- 25
8 capable of emitting light at a first wavelength
9 maximum when chemically treated;
- 10 c. contacting said Lumi-M-P compound with said binding
11 complex to allow the enzymatic reaction of claim 30 to
12 occur for the generation of said Lumi-M capable of
13 emitting light at a second wavelength maximum when
14 chemically treated;
- 15 d. detecting said emitted lights selectively or
16 individually as an indication of the presence and/or
17 amount of said analyte.

1 41. A method for the detection and/or quantitation of a
2 hydrolytic enzyme in a sample comprising the steps of :

- 3 a. providing an enzymatically hydrolyzable chemi-
4 luminescent Lumi-M-P selected from claims 26-29
5 capable of emitting light within a first time interval
6 when chemically treated;
- 7 b. contacting said Lumi-M-P compound with said sample
8 containing said enzyme to allow the enzymatic reaction
9 of claim 30 to occur for the generation of said Lumi-M

10 capable of emitting light within a second time
11 interval when chemically treated; and
12 c. detecting said emitted lights within said first time
13 interval or within said second time interval to
14 discern the change in the light intensity as an
15 indication of the presence and/or the amount of said
16 enzyme.

Cont
a' 1 42. An assay method for the detection and/or quantitation of an
2 analyte in a sample comprising the steps of:
3 a. combining said sample with at least a member of
4 binding pair labeled with a hydrolytic enzyme to form
5 a binding complex;
6 b. providing an enzymatically hydrolyzable chemi-
7 luminescent Lumi-M-P selected from claims 26-29
8 capable of emitting light within a first time
9 interval when chemically treated;
10 c. contacting said Lumi-M-P compound with said binding
11 complex to allow the enzymatic reaction of claim 30 to
12 occur for the generation of said Lumi-M capable of
13 emitting light within a second time interval when
14 chemically treated; and
15 d. detecting said emitted lights within said first time
16 interval or within said second time interval to
17 discern the change in the light intensity as an
18 indication of the presence and/or amount of said
19 analyte.

In the specification:

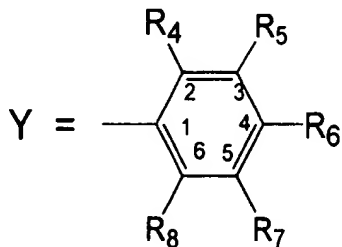
1. Please change the title of the application to read:

a² CHEMILUMINESCENT SUBSTRATES OF HYDROLYTIC ENZYMES

2. Please correct the Formula III overlapping pages 26-27 and its placement so that page 26, line 17-page 27 line 7 read as follows:

X is nitrogen, oxygen or sulfur.

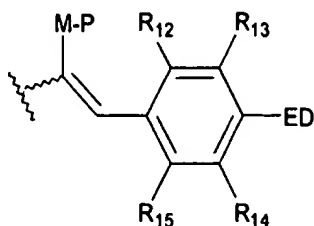
When X is oxygen or sulfur, Z is omitted and Y is a substituted or unsubstituted aryl group, and preferably Y is a polysubstituted aryl group of the formula III:



Formula III

As shown in Formula III, R₄ and R₈ may be identical or

3. Please correct the Formula X overlapping pages 46-47 to appear as follows:



Formula X

4. On page 57, line 26, please insert -Kricka,- before "Clin.". The name of the author of the reference was omitted.
5. On page 60, line 4, please delete "1990" and insert -1980- therefor to correct the publication date of the reference.
6. Please move the figures representing the reaction scheme from the bottom of page 84 to page 85, line 4, following the title of Example 10.
7. On page 86, line 28, please change the number in parenthesis from "11" to -12-. On page 87, line 16, please change the number in parenthesis from "12" to -11-.

REMARKS

1. Before examination of this application, please amend the application as shown above.
2. None of the amendments introduce new matter, as shown by the citations in the following table:

| <u>Claim</u> | <u>Supported by</u> |
|--------------|--|
| 21 | Page 31, Formula VI |
| 22 | Figure 1K; Figure 2K; page 85, Example 10 |
| 23 | Page 49, Formula XII and Page 46, Formula X |
| 24 | Page 47, lines 16-27 |
| 25 | Page 49, Structure 13; Fig. 1M; page 88, Example 11 |
| 26 | Page 53, Formula XIII |
| 27 | Page 53, lines 14-15 |
| 28 | Page 53, lines 15-16 |
| 29 | Page 54, Structure 17; Fig. 1Q; Figure 2-O; page 100, Example 15 |
| 30 | Page 12, lines 1-12; pages 101-103, Examples 16-18 |
| 31 | Page 12, lines 12-17 |
| 32 | Page 12, lines 7-9 |
| 33 | Page 14, lines 16-29; Page 40, line 3-page 41, line 4 |
| 34 | Page 14, lines 16-19 |
| 35 | Page 46, lines 11-15; Page 15, lines 1-21; |

- Page 14, lines 22-25
- 36 Page 40, line 3-page 41, line 4; Page 15,
lines 1-12
- 37 Page 14, lines 20-22; page 15, lines 12-
16; page 46, lines 6-15
- 38 Page 42, lines 16-22
- 39 Page 15, line 22-page 16, line 8; page
57, line 1-page 62, line 5; page 101, line
17-page 103, line 25
- 40 Page 15, line 22- page 16, line 8; page 57,
line 1-page 62, line 5; page 105, line 12-
page 110, line 4
- 41 Page 15, line 22-page 16, line 8; page 57,
line 1-page 62, line 5; page 103, Example
18; Figure 13
- 42 Page 15, line 22- page 16, line 8; page 57,
line 1-page 62, line 5

Correction in
specification

Formula III

Supported by

Much of the structure is shown in the specification. See also Claim 9; also see Formula III on page 19 in Provisional Application Ser. No. 60/146,648, filed 7/30/99, which is the priority application for the instant application.

Formula X

Much of the structure is shown in the specification; see also page 47, line 4-page 49, line 3, including Formulas XI and XII. See also Provisional Application Ser. No. 60/146,648, filed 7/30/99, which is the priority application for the instant application, on page 33.

Example 10

In the title of Example 10 on page 85, lines 2-3, the numbers used to identify 2-OH-Spiroacridine and 2-Phos-Spiroacridan were 12 and 11, respectively. In the discussion of these 2 compounds on page 86, line 28 and page 87, line 16, the numbers 11 and 12 were reversed. This amendment corrects the numbers on pages 86 and 87 so that they are now consistent with the title.

3. Please note that, under separate cover, the correspondence address for this application has been changed to the following:

Patrick Iggoe
Patent Counsel
Bayer Corporation
511 Benedict Avenue
Tarrytown, NY 10591-5097

-14-

Tel. 914-524-2684

Fax 914-524-3594

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter which would expedite allowance of the present application.

Respectfully submitted,

QINGPING JIANG ET AL.

By: Arthur S. Morgenstern
Arthur S. Morgenstern
Registration No. 28,244
Attorney for Applicants

WEINGARTEN, SCHURGIN,
GAGNEBIN & HAYES LLP

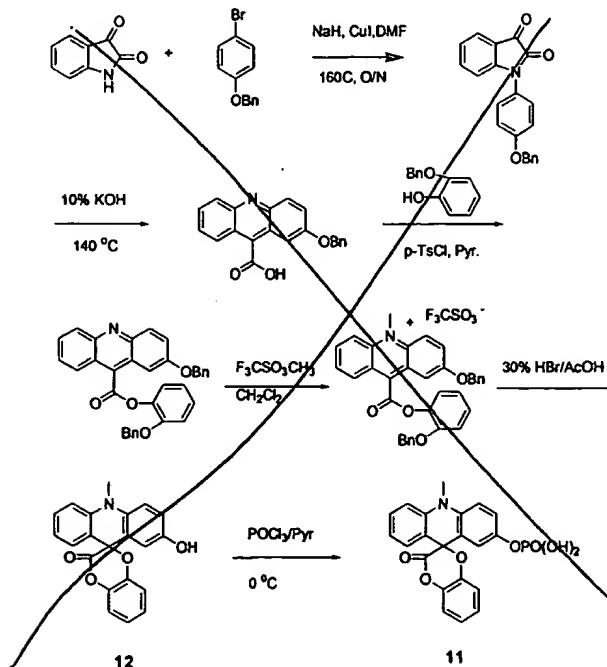
Ten Post Office Square
Boston, MA 02109
Telephone: (617) 542-2290
Telecopier: (617) 451-0313

Dated: 11/8/00

ASM/jds
232020v3

Synthesis of (2',6'-dimethyl-4'carboxyl)phenyl 2-phos-
phoryloxy-7-methoxy-10-methyl-acridinium-9-carboxylate (9)

Crude deblocked acridinium ester from above (80 mg) was dissolved in pyridine (25 ml) and treated with phosphorus oxychloride (3 x 75 μ l, ~15 equivalents) at 0°C under nitrogen. The reaction was stirred for 1 hour and then quenched with water (3 ml) and stirred for an additional hour at room temperature. The reaction was then concentrated to a small volume. HPLC analysis using the same conditions as above but with a 40-minute gradient of 10-60% acetonitrile/water (each with 0.05% TFA) showed product eluting at 20 minutes with starting material eluting at 24 minutes. The product was isolated by preparative HPLC and the HPLC fractions were lyophilized to dryness. Yield = 3 mg yellow powder. MALDI-TOF MS 513.00 obs. (513.26 calc.)



Example 10.

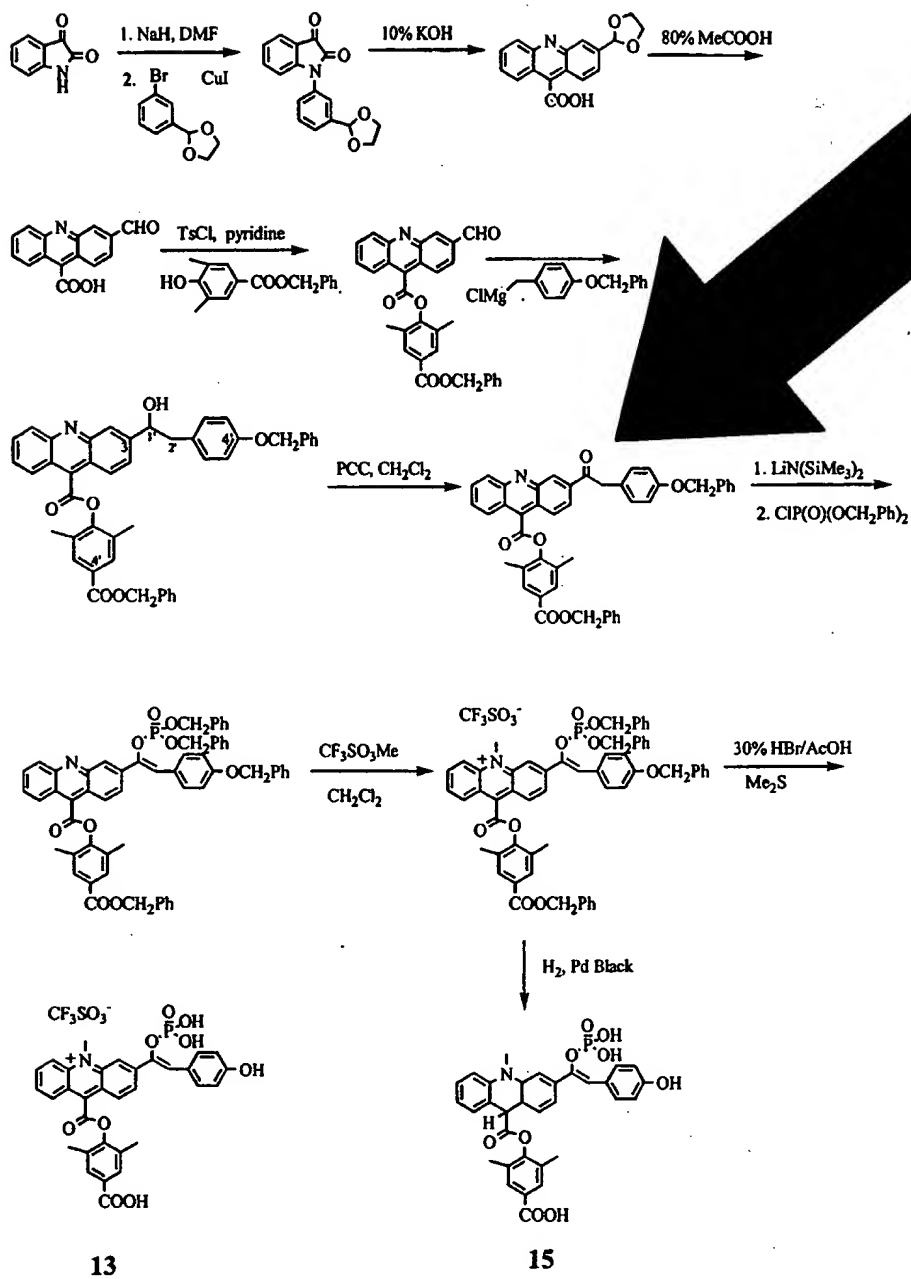
Synthesis of 2-OH-Spiroacridan (12) and 2-Phos-Spiroacridan (11)

5 N-(4'-Benzyloxy)phenylisatin

To a solution of isatin (4 g, 27.2 mmol) in DMF (50 ml) under nitrogen at room temperature was added NaH (871 mg, 34.5 mmol). The reaction color changed from orange to purple. It was stirred at room temperature for 30 min before 4-benzyloxyphenyl bromide (10.21 g, 38.8 mmol) and CuI (10.34 g, 54.4 mmol) were added. It was refluxed at 160 °C in an oil bath for 20 hours under nitrogen. After cooling to room temperature, the reaction was poured into chloroform (400 ml), and filtrated. The filtrate was concentrated to dryness under reduced pressure to give the desired product as a brown gum. It was used in the next step without further purification.

2-Benzyloxyacridine-9-carboxylic acid

The above mixture in 10% KOH/H₂O (220 ml) was refluxed at 130°C for 20 hours. The reaction was filtered while warm, and the filtrate was cooled to 0°C before it was acidified with concentrated HCl to pH 3. The yellow precipitate was filtered, and the filter cake was washed with water (4 x 200 ml). It was dried under reduced pressure at 50°C for 20 hours. The desired product was obtained in 1.8 g. It was confirmed by MS (MALTI-TOF): m/z 331 (M + 1).



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INTELLECTUAL PROPERTY LAW
PATENTS, TRADEMARKS AND COPYRIGHTS

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(617) 451-0313

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GROUP 1600

OFFICIAL

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OF COUNSEL
ARTHUR S. MORGENSTERN

JOSEPH WEINGARTEN
(1919-1984)

FACSIMILE COVER SHEET

DATE: August 14, 2003

TO: Examiner Gitomer
Group Art Unit: 1651 *

Fax No.: (703) 308-4556

FROM: Arthur S. Morgenstern

No. of pages transmitted
(including this page) 31

Our File: CCDLT-300XX

Time:

Your Ref: Appl. No. 09/626,566
Filed: July 27, 2000

Sent by: Leigha

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MESSAGE

PLEASE DELIVER DIRECTLY TO:
EXAMINER GITOMER, Tel. (703) 308-0732
GROUP ART UNIT NO: 1651

FOR ENTRY

Enclosed for filing please find an: AMENDMENT

The Commissioner is hereby authorized to Charge Deposit
Account No. 23-0804 for any additional filing fees associated
with this communication or credit any overpayment.


Attorney for Applicant: Arthur S. Morgenstern
Registration No. 28,244

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RECIPIENT(S). THANK YOU.

Application No.: 09/626,566
 Filed: July 27, 2000
 Group Art Unit: 1651

Rev 05/03

WEINGARTEN, SCHURGIN, GAGNEBIN & LEBOVICI LLP
 Ten Post Office Square
 Boston, Massachusetts 02109
 Telephone: (617) 542-2290
 Telecopier: (617) 451-0313

Date: August 14, 2003

Via Facsimile

COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, VA 22313-1450

Attorney

Docket No.: CCDLT-300XX

Sir:

In re application of: Quingping Jiang, et al.

Entitled: **NOVEL CHEMILUMINESCENT SUBSTRATES OF HYDROLYTIC ENZYMES AND THEIR USE IN ASSAYS**

Transmitted herewith is an amendment in the above-identified application. The following checked items are applicable:

- ☐ This is a Request for Continued Examination under §1.114; authorization is provided herewith to charge Deposit Account No. 23-0804 for the cost of same (\$) per §1.17(e).
☐ Enter the unentered amendment previously filed on _____ per §1.116.
- ☐ A Petition for Extension of Time for _____ month is hereby made under §1.136(a); authorization is provided herewith to charge Deposit Account No. 23-0804 for the cost of same (\$) per §1.17.
- ☒ In the event a Petition for Extension of Time is required by this paper and not otherwise provided, such Petition is hereby made and authorization is provided herewith to charge Deposit Account No. 23-0804 for the cost of such extension.
- ☐ _____ is hereby appointed Associate Attorney by:
 Registration No.:

Attorney of Record:
 Registration No.:

☐ Other:

| CLAIMS AFTER AMENDMENT: | MINUS PRIOR PAID CLAIMS: | EQUALS PRESENT EXTRA CLAIMS: | RATE: | ADDITIONAL FEE: |
|---|--------------------------|------------------------------|--------------|-----------------|
| Independent | 11 - 10 | = 1 | x \$84.00 = | 84.00 |
| Total | 23 - 46 | = 0 | x \$18.00 = | 0 |
| <input type="checkbox"/> Multiple Dependent Claims (1st presentation) | | | + \$280.00 = | 0 |
| SUBTOTAL ADDITIONAL FEE | | | | 84.00 |
| Small Entity filing, divide by 2. Small Entity status must be asserted. | | | | 0 |
| TOTAL ADDITIONAL FEE | | | | 84.00 |

- ☐ No additional fee. ☒ The fee has been calculated above; authorization is provided herewith to charge Deposit Account No. 23-0804 (\$84.00) for the cost of same.
- ☒ The Commissioner is hereby authorized to charge payment of any additional filing fees under §1.16 associated with this communication or credit any overpayment to Deposit Account No. 23-0804.

I hereby certify that this correspondence is being sent via facsimile to Examiner Gitomer, Group Art Unit 1651, Fax No. (703) 308-4556, on 8/14/03.

SUBMIT IN TRIPLICATE
 294843

Arthur S. Morgenstern
 Attorney of Record: Arthur S. Morgenstern
 Registration No.: 28,244

PATENT

Rev 05/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application : Quingping Jiang et al
Application No. : 09/626,566
Filed : 7/27/00
For : NOVEL CHEMILUMINESCENT SUBSTRATES OF
HYDROLYTIC ENZYMES AND THEIR USE IN ASSAYS
Examiner : Ralph J. Gitomer
Attorney's Docket : CCDLT-300XX

Group Art Unit: 1651

I hereby certify that this correspondence is being sent via facsimile to
Examiner R. Gitomer, Group Art Unit 1651, Fax No. (703) 308-4556, on
8/14/03.

By:



Arthur S. Morgenstern

Registration No. 28,244

Attorney for Applicant(s)

AMENDMENT

Via Facsimile
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action dated June 4, 2003, please
amend the above-identified patent application as follows.

DEJIMARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL. (617) 542-2290
FAX. (617) 451-0313

Application No. 09/626,566
Filed: July 27, 2000
Group Art Unit: 1651

AMENDMENTS TO THE SPECIFICATION

1. Please amend the Abstract as follows:

A chemiluminescent substrate of hydrolytic enzyme having the following general Formula I, as follows:

Lumi-M-P

Formula I

where "Lumi" is a chemiluminescent moiety capable of producing light (a) by itself, (b) with MP attached and (c) with M attached. Examples of Lumi includes, but is not limited to, chemiluminescent acridinium compounds ~~(e.g. acridinium esters, acridinium carboxyamides, acridinium thioesters and acridinium oxime esters),~~ benzacridinium compounds, quinolinium compounds, isoquinolinium compounds, phenanthridinium compounds, and lucigenin compounds, ~~or the reduced (e.g., acridans) or non-N-alkylated forms (e.g., acridines) of the above, spiroacridan compounds, luminol compounds and isoluminol compounds and the like.~~ M is a multivalent heteroatom having at least one lone pair of electrons selected from oxygen, nitrogen and sulfur, directly attached to the light emitting moiety of Lumi at one end and to P at the other end. ~~(When M alone is attached to Lumi to form Lumi-M, it does, of course, have either a proton or a counterion associated with it or is in the form of an ion.).~~ P is a group that can be readily removed by hydrolytic enzymes, ~~as discussed in more detail hereinafter.~~ ~~The light emitting moiety of Lumi is well known. For example, when Lumi is an~~

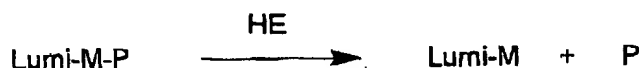
Application No. 09/626,566

Filed: July 27, 2000

Group Art Unit: 1651

~~acridinium compound or luminol, the light emitting moiety is the acridinium nucleus or phthaloyl moiety, respectively.~~

An enzymatic reaction utilizing the above compound is the following ~~having the following general reaction A, as follows:~~



Reaction A

~~where HE is a hydrolytic enzyme, such as phosphatase, glycosidase, peptidase, protease, esterase, sulfatase and guanidinobenzoate.~~
~~Lumi-M-P is a chemiluminescent substrate of a hydrolytic enzyme.~~
Lumi-M is a chemiluminescent product having physical and/or chemical properties different from those of Lumi-M-P. Said ~~physical and/or chemical properties include emission wavelength, quantum yield, light emission kinetics, fundamental net charge distribution, dipole moment, π bond orders, free energy, or apparent hydrophobicity/ hydrophilicity, solubility, affinity and other properties.~~

Application No. 09/626,566

Filed: July 27, 2000

Group Art Unit: 1651

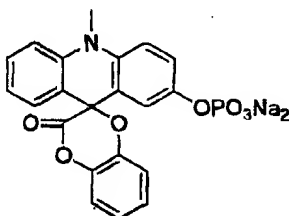
AMENDMENT TO THE CLAIMS

1-7. (Cancelled)

8. (Currently amended) The chemiluminescent substrate of claim 43 wherein said counter ions A are selected from the group consisting of CH_3SO_4^- , FSO_3^- , CF_3SO_3^- , $\text{C}_4\text{F}_9\text{SO}_3^-$, $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

9-21. (Cancelled)

22. (Currently amended) The chemiluminescent substrate of claim 21 having the following structure:



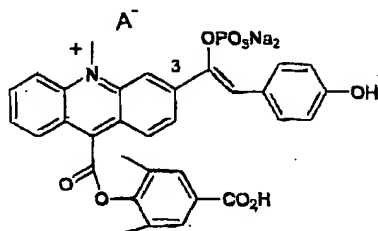
23-24. (Cancelled)

25. (Currently amended) The ~~A~~ chemiluminescent substrate of claim ~~23~~ having the following structure:

Application No. 09/626,566

Filed: July 27, 2000

Group Art Unit: 1651

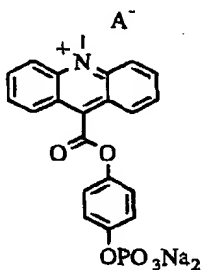


wherein A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said counter ion A^- is selected from the group consisting of $CH_3SO_3^-$, FSO_3^- , $CF_3SO_3^-$, $C_4F_9SO_3^-$, $CH_3C_6H_4SO_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

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26-28. (Cancelled)

29. (Currently amended) ~~The~~ A chemiluminescent substrate ~~of~~
~~claim 26~~ having the following structure:



wherein A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said counter ion A^- is selected from the group consisting of $CH_3SO_3^-$, FSO_3^- , $CF_3SO_3^-$, $C_4F_9SO_3^-$, $CH_3C_6H_4SO_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

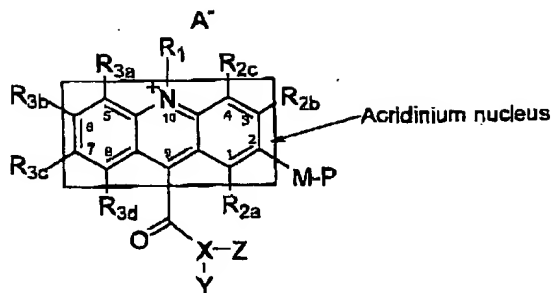
30-42. (Cancelled)

43. (Currently amended) ~~The~~ A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure

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wherein

P is PO_3Na_2 or a sugar moiety;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl and sulfobutyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , are hydrogen;

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted; and

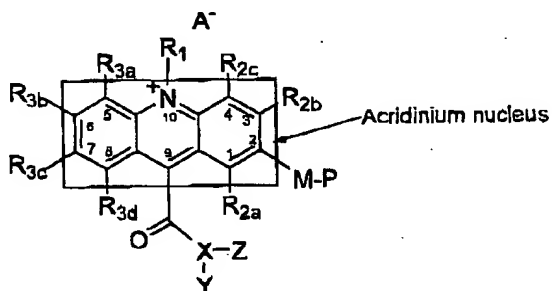
when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

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44. (Currently amended) ~~The~~ A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure,



wherein

P is PO_3Na_2 or a sugar moiety;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl and sulfobutyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , are hydrogen;

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

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X is O; Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted.

45. (Previously added) The chemiluminescent substrate of claim 43, wherein

P is PO_3Na_2 ;

X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

46. (Previously added) The chemiluminescent substrate of claim 43, wherein

P is PO_3Na_2 ;

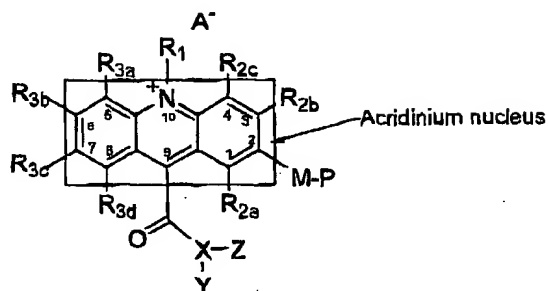
X is S; Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted.

47. (New) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure

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wherein

P is PO_3Na_2 or a sugar moiety;

M is oxygen;

R_1 is selected from the group consisting of sulfoalkyl and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , can be the same or different, selected from the group consisting of hydrogen, methyl, methoxy, halides, and cyano ($-\text{CN}$);

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-

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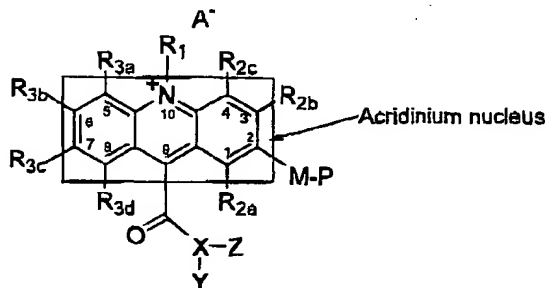
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benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-
benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-
benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl,
(2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-
carboxyl)phenyl;; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

48. (New) The chemiluminescent substrate of claim 47 wherein said counter ions A^- are selected from the group consisting of $CH_3SO_4^-$, FSO_3^- , $CF_3SO_3^-$, $C_4F_9SO_3^-$, $CH_3C_6H_4SO_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

49. (New) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

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P is selected from the group consisting of PO_3H_2 , PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg and $\text{C}(=\text{O})\text{R}$ group wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl, sulfobutyl, sulfoalkyl, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, and cyano ($-\text{CN}$);

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

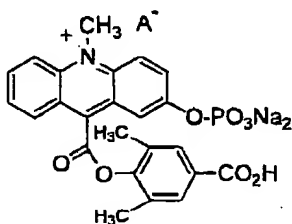
when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl,

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(2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl;; and Z is omitted; and
 when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

50. (New) The chemiluminescent substrate of claim 49 wherein said counter ions A⁻ are selected from the group consisting of CH₃SO₄⁻, FSO₃⁻, CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻, and NO₃⁻.

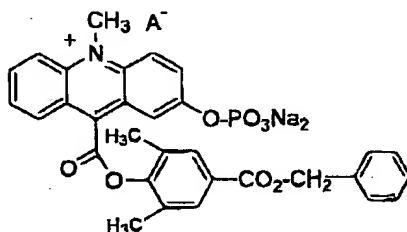
51. (New) The chemiluminescent substrate of Claim 43 having the structure,



wherein A⁻ is selected from the group consisting of CH₃SO₄⁻, FSO₃⁻, CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻, and NO₃⁻.

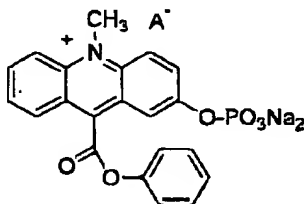
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52. (New) The chemiluminescent substrate of Claim 43 having the structure,



wherein A⁻ is selected from the group consisting of CH₃SO₄⁻, FSO₃⁻, CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻, and NO₃⁻.

53. (New) The chemiluminescent substrate of Claim 43 having the structure,



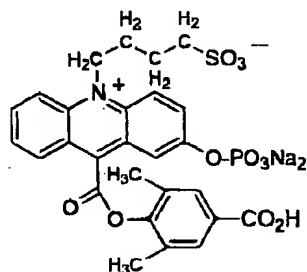
wherein A⁻ is selected from the group consisting of CH₃SO₄⁻, FSO₃⁻, CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻, and NO₃⁻.

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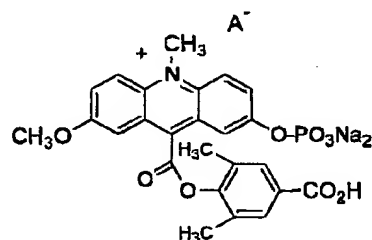
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54. (New) The chemiluminescent substrate of Claim 43 having the structure



55. (New) The chemiluminescent substrate of Claim 47 having the structure,



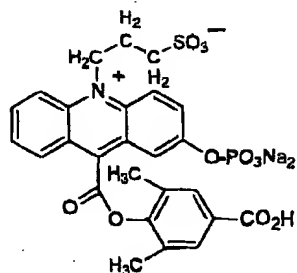
wherein A- is selected from the group consisting of CH_3SO_4^- , FSO_3^- , CF_3SO_3^- , $\text{C}_4\text{F}_9\text{SO}_3^-$, $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

56. (New) The chemiluminescent substrate of Claim 43 having the structure

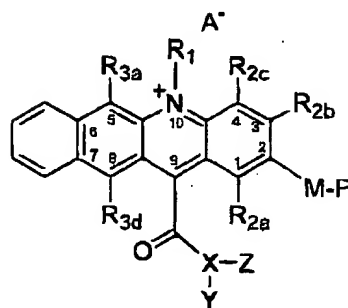
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57. (New) A chemiluminescent substrate of having the structure



wherein

P is selected from the group consisting of PO_3H_2 ,

PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group

wherein R is an alkyl group having 1 to 6 carbon atoms;

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M is oxygen;

R₁ is selected from the group consisting of methyl, sulfopropyl, sulfoethyl, sulfoalkyl, and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3a}, and R_{3d}, can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, cyano (-CN), ;

A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl;; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

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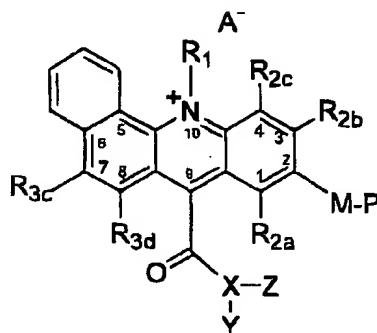
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58. (New) A chemiluminescent substrate having the structure



wherein

P is selected from the group consisting of PO_3H_2 , PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group

wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl, sulfobutyl, sulfoalkyl, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3c} and R_{3d} , can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, and cyano ($-\text{CN}$);

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being

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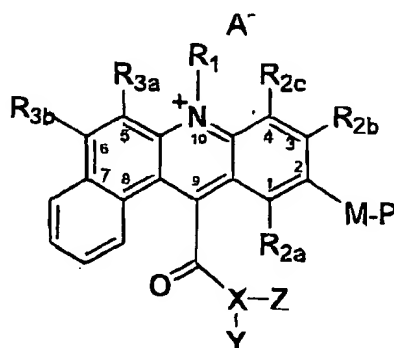
present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl,; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

59. (New) A chemiluminescent substrate having the structure



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wherein

P is selected from the group consisting of PO_3H_2 , PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl, sulfobutyl, sulfoalkyl, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , and R_{3b} can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, cyano ($-\text{CN}$), ;

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-

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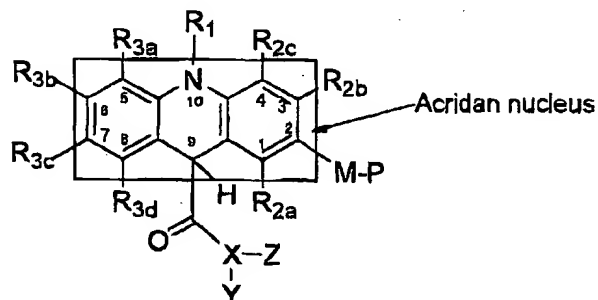
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benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl,
 (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-
 carboxyl)phenyl,; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

60. (New) A chemiluminescent substrate of a hydrolytic enzyme,
 said substrate having the structure



wherein

P is selected from the group consisting of PO_3H_2 , PO_3K_2 ,
 $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group
 wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

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R₁ is selected from the group consisting of methyl, sulfoethyl, sulfoethyl, sulfoethyl, sulfoethyl, and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3a}, R_{3b}, R_{3c} and R_{3d}, can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, cyano (-CN), ;

A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N or S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl,; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

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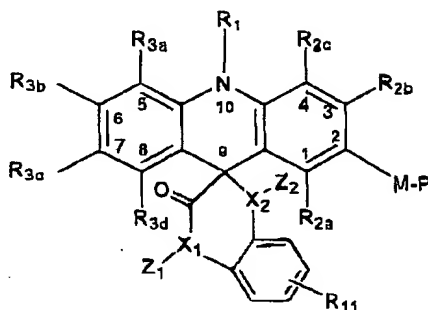
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61. (New) A chemiluminescent substrate of a hydrolytic enzyme,
said substrate having the structure



wherein

P is selected from the group consisting of PO_3H_2 , PO_3K_2 , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and $\text{C}(=\text{O})\text{R}$ group wherein R is an alkyl group having 1 to 6 carbon atoms;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl, sulfobutyl, sulfoalkyl, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} , can be the same or different, selected from a group consisting of hydrogen, methyl, methoxy, halides, cyano ($-\text{CN}$), ;

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group

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that can form an anion and pair with the quaternary ammonium cationic moiety; and

X_1 and X_2 are the same or different and are selected from the group consisting of O, N or S, such that,

when X_1 and X_2 are O or S, R_{11} is selected from the group consisting of hydrogen, -R, substituted or unsubstituted aryl, halides, nitro, sulfonate, sulfate, phosphonate, $-CO_2H$, $-C(O)OR$, cyano (-CN), -SCN, -OR, -SR, -SSR, $-C(O)R$, $-C(O)NHR$, ethylene glycol, or polyethylene glycol, where R is as defined above; and Z_1 and Z_2 are omitted; and

when at least one of X_1 and X_2 is N, Z_1 and Z_2 are toluenesulfonyl, and R_{11} is carboxypropyl.

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REMARKS

1. This is in response to the Office Action mailed June 4, 2003. Claims 8, 22, 25, 29 and 43-61 remain pending in this application.

2. Applicant appreciates the courtesy extended by the Examiner in allowing a telephone interview on August 7, 2003. Participating in the interview were Examiner Ralph J. Gitomer, Qingping Jiang (co-inventor) and Arthur S. Morgenstern (Attorney of Record). At the interview, it was agreed that the scope of Group I, the elected Group of claims, should be expanded. However, the Examiner had difficulty in searching many of the claims in Group I aside from claims 43-46. Applicant agreed to draft other claims in Group I that could be searched to replace those that were difficult to search.

In an attempt to simplify the searching needed, Applicant is introducing new claims 47-61 and has amended claims 8, 22, 25 and 29, all of which are intended to be in Group I. Applicant requests that, if the Examiner has difficulty in searching these new claims, he contact Applicant. Applicant has cancelled claims 1-7, 9-21, 23-24 and 26-28 in Group I but reserves the right to reinstate these claims as the prosecution proceeds.

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3. Applicant has cancelled claims 30-42, which are in Groups II, III and IV.

4. Applicant requests reconsideration of the rejections under 35 USC 112, second paragraph.

a. As indicated above, Applicant intended that claims 43-46 be examples of the claims in Group I. Claim 43 defines MP to be PO_3Na_2 . The methoxy substituent in the R_{3c} position (Figures 1I and 4 (page 10) in the paper filed 5/5/03) is disclosed on page 24, line 23 - page 25, line 13 of the application and is claimed in new claims, including claim 47.

b. Applicant has amended claims 43 and 44 to begin with "A".

5. Applicant had amended the title in the Preliminary Amendment filed 11/8/00 to read CHEMILUMINESCENT SUBSTRATES OF HYDROLYTIC ENZYMES. Applicant believes that this revised title reflects the claims pending and requests reconsideration of the objection to the title.

6. The abstract has been amended as shown above.

7. The description of the structure in Formula I on page 19 of the application (Lumi-M-P) is what was intended to be in the

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original application. The components of the structure were defined in lines 7-17 on page 19. Similarly, in other places in the application, a similar description was used to define the scope of the compounds intended to be covered. (See, for example, Formula I on page 11.)

It should be noted that several typographical errors were corrected in the 11/8/00 Preliminary Amendment, namely the location of Formula III (on pages 26-27 of the application) and Formula X (pages 46-47).

8. In response to the request from the Examiner, Applicant would like to point out that there is support in the original application for claims 43-46, as shown in the following table:

| | |
|--------------------------------------|---|
| General structure | P. 23, Formula II |
| P is PO ₃ Na ₂ | P. 34, fig 1 |
| P is sugar | P. 22, lines 6-9 - these are enzymes that react in Reaction A (P. 12), which implies that the sugar must be part of the substrate; and this is the only place in the substrate where the sugar could be located |
| M is O | P. 24, lines 4-6 |

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R1 is methyl P. 24, line 15

R1 is sulfobutyl Fig. 1G

R1 is sulfopropyl P. 24, line 16, which defines the
preferred groups as sulfoalkyl

R_{2a} etc are hydrogen P. 24, lines 23-24; P.25, lines 4-5

A- is counterion P. 26, lines 3-16

X is O, N or S P. 26, line 17

Variations when X is O, N, S P. 26, line 17-P. 29, line 13

Note that there is additional support in the application for the claims. Some of this additional support was identified in the table submitted on April 2, 2003.

9. Support for the new substrate claims also can be found in the original application. For example,

claims 57-59 Formulas on top 2 lines of page 21

claim 60 Formula IV on page 30; page 29 lines 14-22

claim 61 Formula VI on page 31 of the application; page 30,
line 4 through page 31, line 10

10. Applicant notes that two Information Disclosure Statements have been filed in this application. The first was filed November

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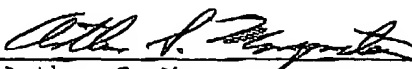
Application No. 09/626,566
Filed: July 27, 2000
Group Art Unit: 1651

8, 2000 and the second filed March 12, 2001. Please provide acknowledgements of the PTO-1449's for these IDS's.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

QINGPING JIANG ET AL

By: 
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TC Art Unit: 1651**Fax No.:** (703) 872 9306**FROM:** Holliday C. Heine, Ph.D.**No. of pages transmitted
(including this page):** 27**Our File:** CCDLT-300XX**Time:****Your Ref:****Sent by:** Holly

Application No. 09/626,566

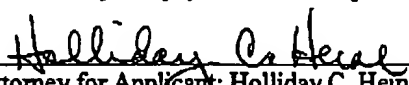
Filed Date: July 27, 2000

Confirmation No.: 9704

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MESSAGE**PLEASE DELIVER DIRECTLY TO:****EXAMINER** Ralph J. Gitomer, Tel. (703) 308 0732
TC ART UNIT NO: 1651**FOR ENTRY**

Enclosed for filing please find a: Response to Final Office Action

The Commissioner is hereby authorized to Charge Deposit Account No. 23-0804 for any additional filing fees associated with this communication or credit any overpayment.


Attorney for Applicant: Holliday C. Heine, Ph.D.
Registration No. 34,346

302326-1

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application : Qingping Jiang et al.
Application No. : 09/626,566
Filed : July 27, 2000
Confirmation No. : 9704
For : NOVEL CHEMILUMINESCENT SUBSTRATES OF
HYDROLYTIC ENZYMES AND THEIR USE IN ASSAYS
Examiner : Gitomer, Ralph J.
Attorney's Docket : CCDLT-300XX

Group Art Unit: 1651

I hereby certify that this correspondence is being sent via
facsimile to Examiner Ralph J. Gitomer, Group Art Unit 1651, Fax
No. (703) 872 9306, on Feb. 23, 2004.

By: Holliday C. Heine
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

AMENDMENT PURSUANT TO 37 C.F.R. §1.116

Via Facsimile
After Final
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Final Office Action dated October 23,
2003, please amend the above-identified patent application as
follows.

WEINGARTEN, SCHURGIN,
GARDINER & LEBOWITZ LLP
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FAX (617) 541-2250

Application No. 09/626,566
Filed: July 27, 2000
Group Art Unit: 1651
Confirmation No.: 9704

AMENDMENTS TO THE SPECIFICATION

Please amend the Title of the above-identified application to
read as follows:

CHEMILUMINESCENT ACRIDINIUM COMPOUNDS AND ANALOGUES THEREOF
AS SUBSTRATES OF HYDROLYTIC ENZYMES

Application No. 09/626,566

Filed: July 27, 2000

Group Art Unit: 1651

Confirmation No.: 9704

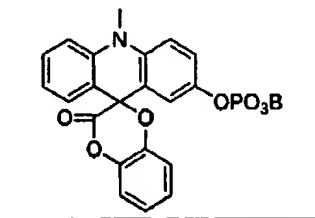
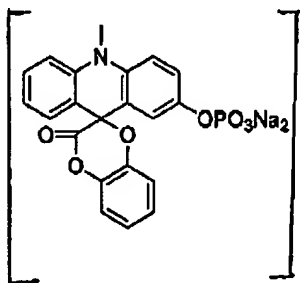
AMENDMENT TO THE CLAIMS

1-7. (Cancelled)

8. (Currently amended) The chemiluminescent substrate of claim 43 wherein said counter ions ~~are~~ anion A⁻ is selected from the group consisting of CH_3SO_4^- , FSO_3^- , CF_3SO_3^- , $\text{C}_4\text{F}_9\text{SO}_3^-$, $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_3^-$, halide, CF_3COO^- , CH_3COO^- , and NO_3^- .

9-21. (Cancelled)

22. (Currently amended) The chemiluminescent substrate of claim 61 having the following structure:



23-24. (Cancelled)

25. (Cancelled)

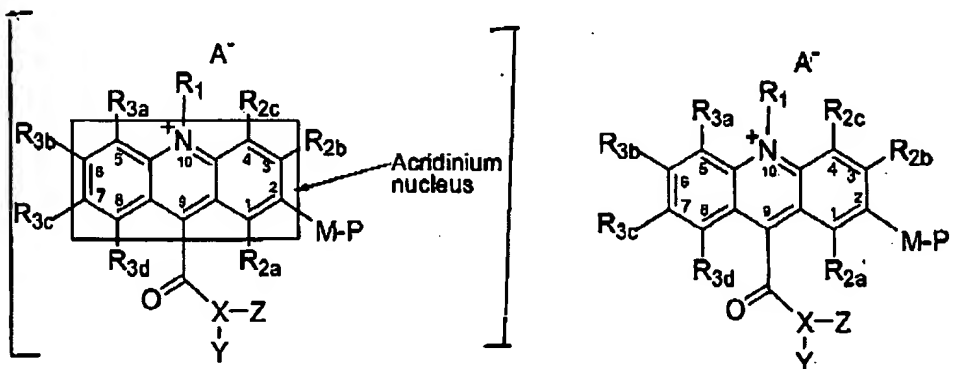
26-28. (Cancelled)

29. (Cancelled)

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30-42. (Cancelled)

43. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

P is PO_2Na_2 - PO_3B or a sugar moiety and B is a divalent cation or two monovalent cations selected from the group consisting of Na_2 , H_2 , K_2 , Ca and Mg ;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfopropyl and sulfobutyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} are hydrogen;

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group

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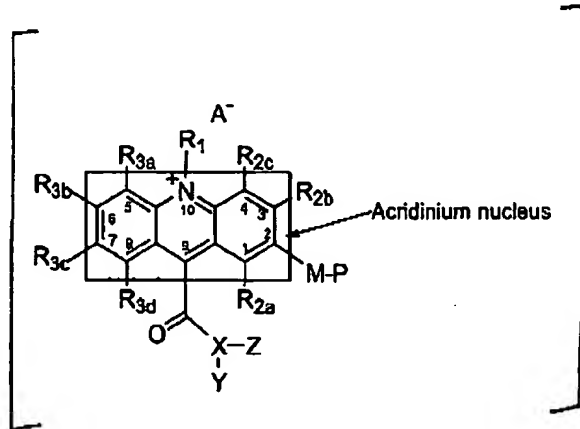
that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N ~~or~~ and S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

44. (Currently amended) A ~~The~~ chemiluminescent substrate of claim 43, wherein ~~a hydrolytic enzyme, said substrate having the structure,~~



wherein

P is PO₃B ~~PO₃Na₂ or a sugar moiety;~~

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~~M is oxygen;~~~~R₁ is selected from the group consisting of methyl, sulfopropyl and sulfobutyl;~~~~R_{2a}, R_{2b}, R_{2c}, R_{2d}, R_{2e}, R_{2f} and R_{2g} are hydrogen;~~~~A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and~~

X is O; Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted.

45. (Currently amended) The chemiluminescent substrate of claim

43, wherein

P is ~~PO₃Na₂~~PO₃B;

X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

46. (Currently amended) The chemiluminescent substrate of claim

43, wherein

P is ~~PO₃Na₂~~PO₃B;

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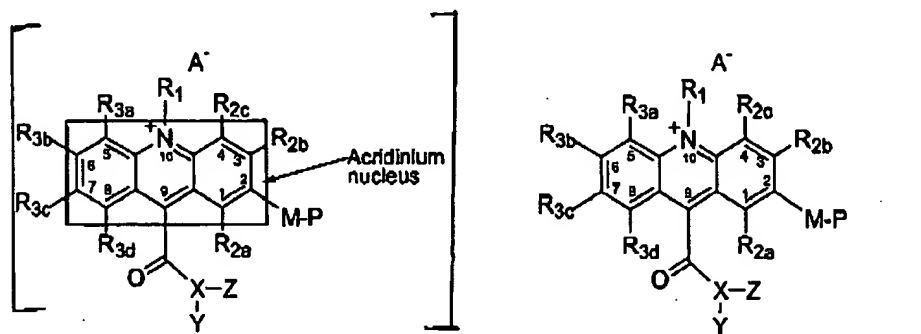
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X is S; Y is selected from the group consisting of phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, and (2',6'-dimethyl-4'-carboxyl)phenyl; and Z is omitted.

47. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



P is PO_3Na_2 , PO_3B or a sugar moiety and B is a divalent cation or two monovalent cations selected from the group consisting of Na_2 , H_2 , K_2 , Ca and Mg;

M is oxygen;

R_1 is selected from the group consisting of methyl, sulfoalkyl and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} , R_{3b} , R_{3c} and R_{3d} can be the same or different, and are selected from the group consisting of hydrogen, methyl, methoxy, halides, and cyano (-CN);

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A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N ~~or~~ and S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl and Y is carboxypropyl.

48. (Currently amended) The chemiluminescent substrate of claim 47 wherein said counter ~~ions-ion~~ A⁻ ~~are-is~~ is selected from the group consisting of CH₃SO₄⁻, FSO₃⁻, CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻, and NO₃⁻.

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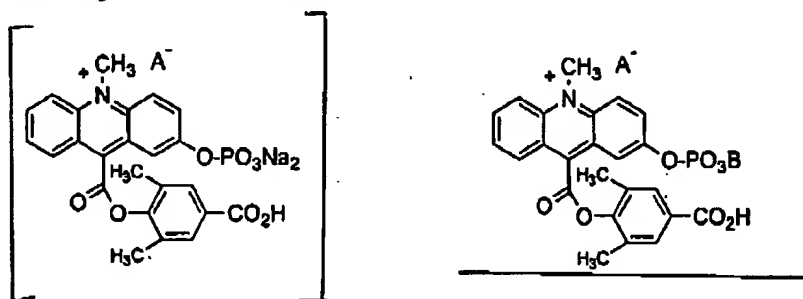
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49. (Cancelled)

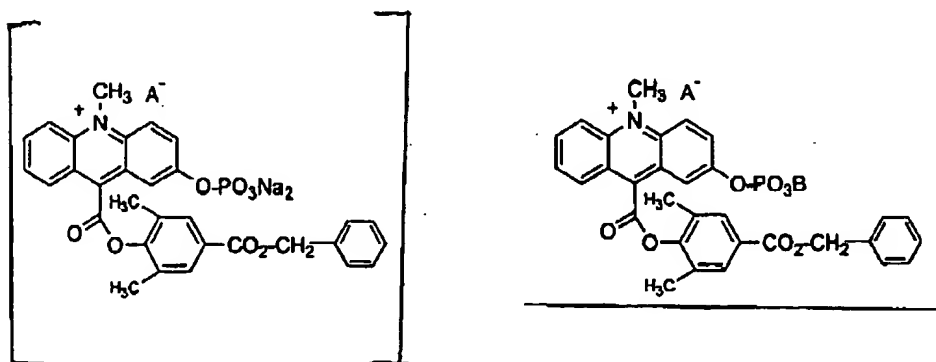
50. (Cancelled)

51. (Currently amended) The chemiluminescent substrate of ~~Claim~~
claim 43 -having the structure-



wherein A⁻ is selected from the group consisting of CH₃SO₃⁻, FSO₃⁻,
 CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻ and NO₃⁻.

52. (Currently amended) The chemiluminescent substrate of ~~Claim~~
claim 43 having the structure-



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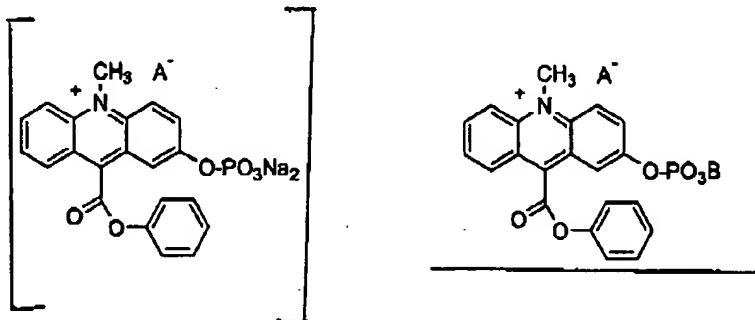
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Group Art Unit: 1651

Confirmation No.: 9704

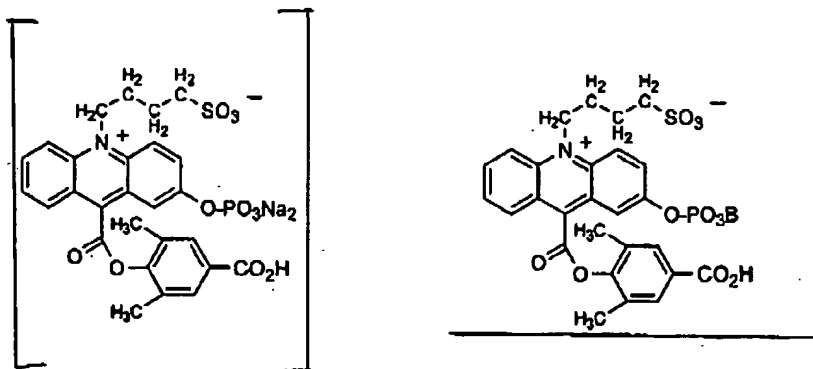
wherein A^- is selected from the group consisting of $CH_3SO_4^-$, FSO_3^- , $CF_3SO_3^-$, $C_4F_9SO_3^-$, $CH_3C_6H_4SO_3^-$, halide, CF_3COO^- , CH_3COO^- and NO_3^- .

53. (Currently amended) The chemiluminescent substrate of ~~claim~~ claim 43 having the structure,



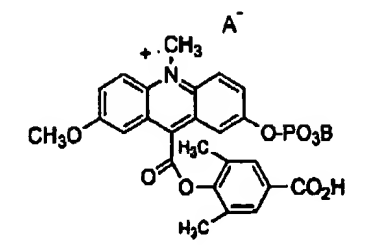
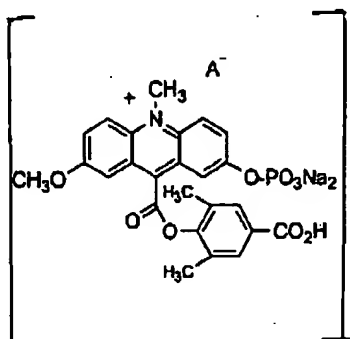
wherein A^- is selected from the group consisting of $CH_3SO_4^-$, FSO_3^- , $CF_3SO_3^-$, $C_4F_9SO_3^-$, $CH_3C_6H_4SO_3^-$, halide, CF_3COO^- , CH_3COO^- and NO_3^- .

54. (Currently amended) The chemiluminescent substrate of ~~claim~~ claim 43 having the structure



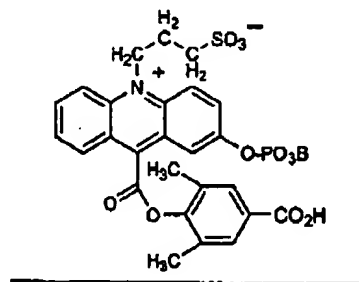
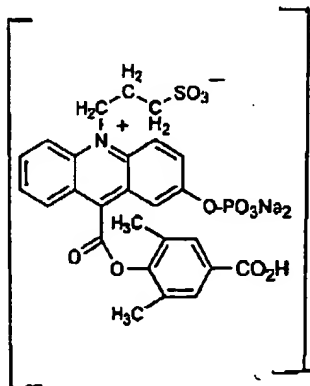
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55. (Currently amended) The chemiluminescent substrate of ~~Claim~~
claim 47 having the structure



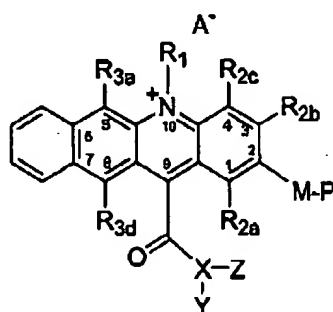
wherein A⁻ is selected from the group consisting of CH₃SO₄⁻, FSO₃⁻,
 CF₃SO₃⁻, C₄F₉SO₃⁻, CH₃C₆H₄SO₃⁻, halide, CF₃COO⁻, CH₃COO⁻ and NO₃⁻.

56. (Currently amended) The chemiluminescent substrate of ~~Claim~~
claim 43 having the structure



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57. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

P is PO₃B or ~~selected from the group consisting of PO₃H₂, PO₃K₂, PO₃(NH₄)₂, PO₃Ca, PO₃Mg, PO₃Na₂~~, a sugar moiety and B is a divalent cation or two monovalent cations selected from the group consisting of Na₂, H₂, K₂, Ca and Mg ~~C(-O)R group wherein R is an alkyl group having 1 to 6 carbon atoms;~~

M is oxygen;

R₁ is selected from the group consisting of methyl, ~~sulfoethyl, sulfoethyl, sulfoethyl~~, and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3a}, and R_{3d} ~~can be the same or different, and~~ are selected from a the group consisting of hydrogen, methyl, methoxy, halides, and cyano (-CN) ~~;~~

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A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

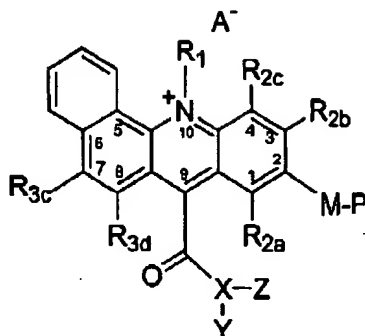
X is selected from the group consisting of O, N ~~or~~ and S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

58. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure

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 Filed: July 27, 2000
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wherein

P is PO₃B or ~~selected from the group consisting of PO₃H₂, PO₃K₂, PO₃(NH₄)₂, PO₃Ca, PO₃Mg, PO₃Na₂, a sugar moiety and B is a~~
divalent cation or two monovalent cations selected from the group
consisting of Na₂, H₂, K₂, Ca and MgC(=O)R ~~group wherein R is an~~
~~alkyl group having 1 to 6 carbon atoms;~~

M is oxygen;

R₁ is selected from the group consisting of methyl,
~~sulfoethyl, sulfoethyl, sulfoalkyl,~~ and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3c} and R_{3d} ~~can be the same or different, and~~
are selected from a the group consisting of hydrogen, methyl,
methoxy, halides, and cyano (-CN)-;

A⁻ is a counter ion for the electroneutrality of the
 quaternary nitrogen of the acridinium compounds, said A⁻ not being
 present if said R₁ substituent contains a strongly ionizable group

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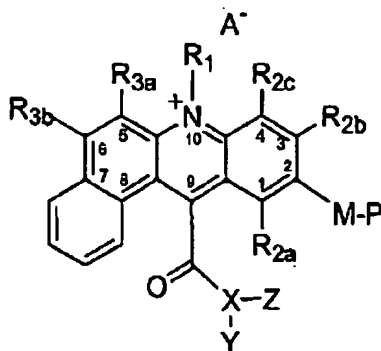
that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N ~~or~~ and S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

59. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



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Filed: July 27, 2000
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wherein

P is PO_3B or ~~selected from the group consisting of PO_3H_2 , PO_3K , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2~~ , a sugar moiety and B is a divalent cation or two monovalent cations selected from the group consisting of Na_2 , H_2 , K_2 , Ca and $\text{MgC}(\text{=O})\text{R}$ ~~group wherein R is an alkyl group having 1 to 6 carbon atoms;~~

M is oxygen;

R_1 is selected from the group consisting of methyl, ~~sulfoethyl, sulfoethyl, sulfoalkyl~~, and carboxymethyl;

R_{2a} , R_{2b} , R_{2c} , R_{3a} and R_{3b} can be the same or different, and are selected from a the group consisting of hydrogen, methyl, methoxy, -halides, and cyano (-CN),

A^- is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A^- not being present if said R_1 substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X is selected from the group consisting of O, N ~~or~~ and S, such that,

when X is O or S, Y is selected from the group consisting of phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-

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Filed: July 27, 2000

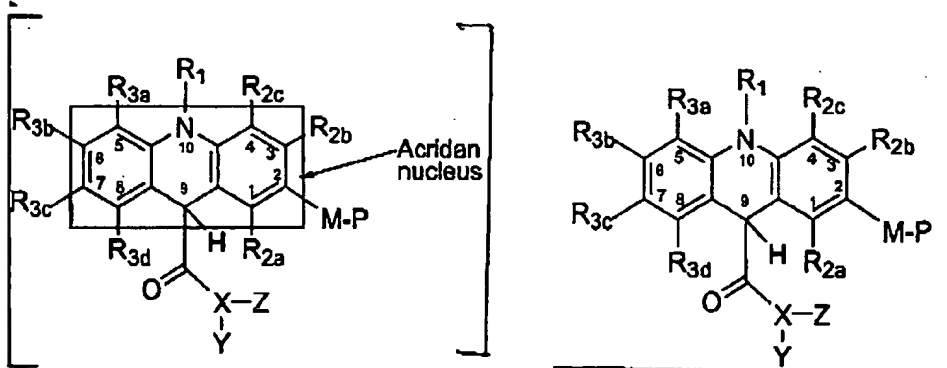
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dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl, (2',6'-dimethoxy-4'-carboxyl)phenyl, and (2'-methyl-6'-methoxy-4'-carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

60. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

P is PO_3B or ~~selected from the group consisting of PO_3H_2 , PO_3K , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na , a sugar moiety and B is a~~ divalent cation or two monovalent cations selected from the group consisting of Na_2 , H_2 , K_2 , Ca and $\text{MgC}(\text{O})\text{R}$ group wherein R is an alkyl group having 1 to 6 carbon atoms;

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M is oxygen;

R₁ is selected from the group consisting of methyl,
~~sulfopropyl, sulfobutyl, sulfoalkyl,~~ and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3a}, R_{3b}, R_{3c} and R_{3d} can be the same or
different, and are selected from a the group consisting of
hydrogen, methyl, -methoxy, halides, and cyano (-CN);

A⁻ is a counter ion for the electroneutrality of the
quaternary nitrogen of the acridinium compounds, said A⁻ not being
present if said R₁ substituent contains a strongly ionizable group
that can form an anion and pair with the quaternary ammonium
cationic moiety; and

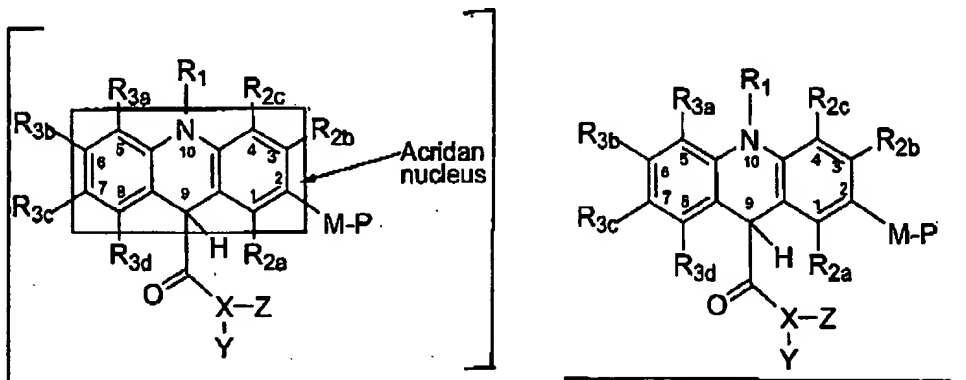
X is selected from the group consisting of O, N ~~or~~ and S,
such that,

when X is O or S, Y is selected from the group consisting of
phenyl, (2'-methyl)phenyl, (2'-methoxy)phenyl, (2',6'-
dimethyl)phenyl, (2'-methyl-6'-methoxy)phenyl, (2',6'-dimethyl-4'-
benzyloxycarbonyl)phenyl, (2',6'-dimethoxy-4'-
benzyloxycarbonyl)phenyl, (2'-methyl-6'-methoxy-4'-
benzyloxycarbonyl)phenyl, (2',6'-dimethyl-4'-carboxyl)phenyl,
(2',6'-dimethoxy-4'-carboxyl)phenyl, ~~and~~ (2'-methyl-6'-methoxy-4'-
carboxyl)phenyl; and Z is omitted; and

when X is N, Z is toluenesulfonyl, and Y is carboxypropyl.

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61. (Currently amended) A chemiluminescent substrate of a hydrolytic enzyme, said substrate having the structure



wherein

P is PO_3B or ~~selected from the group consisting of PO_3H_2 , PO_3K , $\text{PO}_3(\text{NH}_4)_2$, PO_3Ca , PO_3Mg , PO_3Na_2 , a sugar moiety and B is a~~
divalent cation or two monovalent cations selected from the group
consisting of Na_2 , H_2 , K_2 , Ca and $\text{MgC}(-\text{O})\text{R}$ group wherein R is an
alkyl group having 1 to 6 carbon atoms;

M is oxygen;

R₁ is selected from the group consisting of methyl,
~~sulfo~~propyl, ~~sulfo~~butyl, ~~sulfo~~alkyl, and carboxymethyl;

R_{2a}, R_{2b}, R_{2c}, R_{3a}, R_{3b}, R_{3c} and R_{3d} can be the same or
~~different, and are selected from the group consisting of~~
 hydrogen, methyl, methoxy, halides, ~~and cyano (-CN),~~

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R₁₁ is selected from the group consisting of hydrogen, -R, substituted or unsubstituted aryl, halides, nitro, sulfonate, sulfate, phosphonate, -CO₂H, -C(O)OR, cyano (-CN), -SCN, -OR, -SR, -SSR, -C(O)R, -C(O)NHR, ethylene glycol and polyethyelene glycol, where R is an alkyl group having 1 to 6 carbon atoms;

A⁻ is a counter ion for the electroneutrality of the quaternary nitrogen of the acridinium compounds, said A⁻ not being present if said R₁ substituent contains a strongly ionizable group that can form an anion and pair with the quaternary ammonium cationic moiety; and

X₁ -and X₂ -are the same or different and are selected from the group consisting of O, N ~~or~~ and S, such that,

when at least one of X₁ -and X₂ are-is O or S, R₁₁ is selected from the group consisting of hydrogen, -R, substituted or unsubstituted aryl, halides, nitro, sulfonate, sulfate, phosphonate, -CO₂H, -C(O)OR, cyano (-CN), -SCN, -OR, -SR, -SSR, -C(O)R, -C(O)NHR, ethylene glycol, or polyethyelene glycol, where R is as defined above, and the corresponding Z₁ -and-or Z₂ are-is omitted; and

when at least one of X₁ -and X₂ is N, the corresponding Z₁ and or Z₂ are-is hydrogen, alkyl, aryl or toluenesulfonyl, and R₁₁ is carboxypropyl.

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REMARKS

The Applicants respectfully request that the Examiner reinstate claims the withdrawn claims and reconsider the patentability of all the pending claims. Claims 25, 29, 49 and 50 are hereby cancelled. Claims 8, 22, 43-48 and 51-61, as amended above, are submitted as being within the scope of the elected claims. The Applicants stipulate for the record that the patentability of the indicated claims as amended depends on the patentability of the substituent group -M-P and that the remaining portions of the claimed compounds are within the prior art and the skill of the ordinary artisan.

Applicants' cancellation of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicants continue to believe that the rejected claims are described in and enabled by the specification, and are not obvious in view of the cited references. The rejected claims have been cancelled for the sole purpose of advancing the case to allowance. The Applicants reserve the right to file continuing application(s) to continue the prosecution of the rejected claims.

The title has been amended and is believed to be acceptable.

With reference to the IDS's, the Applicants believe that the Examiner can obtain replacement copies of all of the cited patent document references. The Applicants are sending replacement

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copies of all of the cited literature references under separate cover.

The Applicants have carefully amended the remaining claims and believe that they are definite and fully supported in the specification. No new matter has been added. In certain claims, the Applicants have amended the substituent group PO_3Na_2 to read " PO_3B " and have defined B to be a divalent or two monovalent cations selected from the group consisting of Na_2 , H_2 , K_2 , Ca and Mg. In certain claims, the Applicants have amended the ring structure, as indicated.

Thus, the Applicants submit that the indicated claims are in condition for allowance and such action is requested.

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The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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